*Case Report*

# *Saccharomyces cerevisiae* oesophagitis in a patient with oesophageal carcinoma

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**Abstract**
*Saccharomyces* species are emerging opportunistic fungal pathogens that can cause bloodstream infections in humans. These infections have often been associated with the ingestion of probiotics. *Saccharomyces* oesophagitis is a rare condition which has been described so far in only two publications. Here we report the case of a patient who was diagnosed with *Saccharomyces* oesophagitis. The clinical picture was indistinguishable from that of *Candida* oesophagitis. The *Saccharomyces* isolate was shown to be susceptible to fluconazole by both CLSI M27-A and disk diffusion methods. In contrast to cases of fungaemia, *Saccharomyces* oesophagitis does not seem to follow probiotic use. Due to the potential for antifungal resistance among emerging fungal pathogens, proper mycological identification at the species level is essential.

**Key words:** opportunistic infections; oesophagitis; saccharomyces; yeasts; probiotics; cancer.

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## Introduction

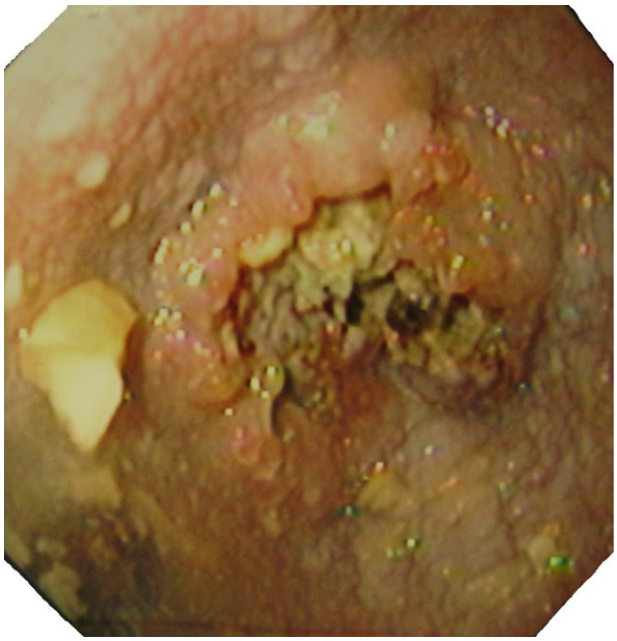
*Saccharomyces* spp. are well-known ubiquitous ascomycetous yeasts used in food business, including baking and brewing industries. Additionally, *Saccharomyces* spp. have been used as nutritional supplements and administered to treat antibiotic-associated diarrhoea [1]. Although these fungi are colonisers of human mucosae [2], a higher number of reports have linked *Saccharomyces cerevisiae* to human infections as an opportunistic agent.

Fungaemia is the most frequent manifestation of *Saccharomyces* infection in humans, mostly associated with contaminated catheters. However, some cases of *Saccharomyces* fungaemia following the use of probiotics have been reported [3]. Other disease manifestations as *Saccharomyces* oesophagitis are rare. Here we describe a case of *Saccharomyces* oesophagitis affecting a patient with oesophageal carcinoma. We used the criteria proposed by Konecny *et al*. to differentiate colonisation from infection [4].

## Case report

A 47-year-old man was admitted to the hospital complaining of a three-month history of progressive dysphagia and weight loss. He gave a history of retrosternal chest pain, nausea, poor appetite, and dyspnoea. During his hospital stay, a single febrile episode was documented (38ºC). Computerised tomography of the chest revealed a dilated oesophagus with a residual liquid content extending to beyond the epiphrenic segment. Thickening of the oesophageal wall was observed, with associated oesophageal obstruction. Oesophagogastroduodenoscopy revealed an exophytic lesion in the upper third of the oesophagus which blocked progression of the endoscope. The mucosa proximal to the vegetant lesion showed white plaques resembling *Candida* oesophagitis. A biopsy was performed, and histopathologic studies revealed the presence of a moderately differentiated epidermoid carcinoma of the oesophagus. In addition to acanthosis and focal areas of necrosis, hyaline

**Figure 1.** Hyperemia and the presence of fungal elements in the upper esophagus.



hyphae were also seen. Direct mycological examination showed presence of yeasts, and fungal culture on Sabouraud-Cloranfenicol at 25ºC revealed growth of *S. cerevisiae.* The fungus was identified at the species level using ID 32C system (bioMeriex, Marcy l'Etoile, France) [5]. Disk diffusion assay using the Clinical and Laboratory Standards Institute (CLSI) reference broth microdilution method M27-A produced a halo of > 30 mm, indicating susceptibility to fluconazole at MIC 0.125 µg/ml) [6]. A 7-day course of fluconazole 400 mg/daily resulted in remission of the clinical symptoms (*i.e.*, retrosternal chest pain, nausea, and dyspnoea). The patient was discharged from the hospital with a plan for further oesophagectomy but he died seven days after leaving the hospital. An autopsy was not performed.

## Discussion

*Saccharomyces* oesophagitis is a rare disease, reported so far in only two publications. Eng *et al*. [7] reported in 1984 that a patient with Waldenstrom's macroglobulinaemia had a mixed oesophageal infection caused by *S. cerevisiae* and *Candida albicans*. The patient received no antifungal therapy and died two days after the diagnosis of causes other than the *Saccharomyces* infection. In another report [4], an HIV-infected patient with *Saccharomyces* oesophagitis was successfully treated with fluconazole. However, no details about sampling procedures and histopathological results were given. The isolate was found to be resistant to itraconazole and showed a high MIC for fluconazole (8 µg/ml). Similarly, in our patient, none of the previous reports associated *Saccharomyces* oesophagitis with the use of probiotics [4, 7]. Although there is no information about the use of probiotics in our case report because the data are from medical records, it is believed that the disease was caused by food ingestion.

*S. cerevisiae* has been increasingly implicated as a human opportunistic pathogen. This probably results not only from improvements in laboratory techniques allowing identification of fungi at the species level, but also from the growing clinical experience achieved in the last decades in the recognition of fungal infections. Moreover, humans are progressively more exposed to *S. cerevisiae* by oral ingestion, because it is believed to be of great nutritional value.

Although *S. cerevisiae* can colonise the oesophageal mucosa without causing infection, the patient described in this report presented all four criteria suggested by Konecny *et al*. to differentiate colonisation from infection [4]. These are (1) presence of clinical symptoms; (2) histopathological evidence for tissue invasion; (3) absence of other organisms recovered in culture; and (4) therapy based on susceptibility tests. In both previous cases of *S. cerevisiae* oesophagitis, these criteria were not

completely fulfilled [4, 7]; therefore, the differentiation between colonisation and infection was not possible.

Due mainly to the low frequency of *Saccharomyces* infections, the best therapeutic approach has not yet been defined. Whilst *S. cerevisiae* has been consistently susceptible to both amphotericin B (MICs of 0.5-1 µg/ml) and 5-flucytosine (0.25 µg/ml), different rates of resistance to fluconazole and itraconazole have been reported [8, 9]. Resistant strains of *Saccharomyces* species can emerge in units where fluconazole is extensively used [10]. Both posaconazole and voriconazole have been reported to have good *in vitro* activity against this fungus [9, 11]. Although the isolate recovered from our patient was susceptible *in vitro* to fluconazole, it should be noted that neither the CLSI nor the disk diffusion method have been formally approved for testing *S. cerevisiae* susceptibility.

In a recent review of the literature [3], 60 cases of *Saccharomyces* fungaemia were found. Interestingly, the majority of cases (54.6%) followed the use of probiotics by a median time of 10 days. It is also of interest that in this review only three patients were healthy before the bloodstream infection (two had self-inflicted fungaemia and one patient ingested large quantities of brewer's yeast as a nutritional supplement). Other clinical syndromes associated with *Saccharomyces* infection included endocarditis, aortic graft infection, tracheo-bronchitis, pneumonia, empyema, liver abscess, peritonitis, vaginitis, urinary tract infection, fever of unknown origin, and cellulites [3].

In conclusion, although *S. cerevisiae* is a rare aetiology of oesophagitis, this opportunistic organism should not be dismissed as non-pathogenic in the presence of the criteria suggested by Konecny *et al*. Since the clinical picture of *Saccharomyces* oesophagitis is indistinguishable from oesophagitis caused by other pathogens, a search for the aetiological agent seems worthy. The emergence of new fungal pathogens in cases of oesophagitis – particularly those with reduced susceptibility to azole anti-fungals – reinforces the importance of proper mycological examination of these samples.

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